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CLINICAL CHARACTERISTICS OF PATIENTS WITH PRECOCIOUS PUBERTY ATTENDING ENDOCRINE UNITS IN MOSUL CITY

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ABSTRACT

Background: Precocious puberty is the abnormal early onset of puberty, defined by the appearance of secondary sexual characteristics before age 8 in girls and before age 9 in boys. It results from either independent sex hormone secretion (peripheral/gonadotropin-independent) or premature activation of the hypothalamic-pituitary-gonadal axis (central/gonadotropin-dependent). **Aim:** To determine the characteristic features and associated factors of children presenting with precocious puberty at endocrine centers in Mosul City. **Methods:** A cross-sectional study was conducted among 94 patients attending the Endocrine Units at Al-Khansa'a Teaching Hospital and Al-Wafa'a Specialized Medical Center between 2 January and 30 June 2025, using a structured questionnaire administered through direct interviews. **Results:** The sample comprised 94 children (78 females. [83%], 16 males. [17%]) aged 1–10 years, with the majority (47.9%) aged 7–8 years; females predominated in younger age groups and males in older groups. Younger girls showed below-average height but elevated weight and BMI Z-scores (Z = +5.6 at age 3), normalizing by age 8, whereas boys showed above-average height and weight in mid-childhood but below-standard values in older ages. Urban residence was common (58.5%), and family history was positive in only 9.6% of cases (all females). Central precocious puberty predominated (74.5%), mostly idiopathic (71.3%); peripheral precocious puberty accounted for 25.5%, primarily congenital adrenal hyperplasia (21.3%). Breast budding was the first sign in 88.5% of females and scrotal enlargement in 62.5% of males. Treatment adherence was high in females (87.2%) but low in males (12.5%). **Conclusion:** Idiopathic central precocious puberty predominates among Mosul's pediatric population, with marked gender disparities in presentation, anthropometric deviations, and treatment adherence, underscoring the need for targeted screening, early intervention, and gender-specific strategies in resource-limited settings.

KEYWORDS: precocious puberty, congenital adrenal hyperplasia, Mosul City, Iraq.

1. INTRODUCTION

Adolescence is the transitional period during which a child matures physically, psychologically, and socially, with puberty representing its initial stage. The hypothalamic-pituitary-gonadal (HPG) axis matures throughout puberty, a complex process accompanied by growth acceleration, development of secondary sexual characteristics, and attainment of fertility.[1] Puberty is a developmental continuum: HPG axis activation begins in utero, is followed by a transient "mini-puberty" of infancy and a subsequent "juvenile pause," before the axis reactivates, typically around age eight in girls and age nine in boys.[2] Early pubertal changes, occurring 2 to 2.5 standard deviations below the mean age of onset (eight to thirteen years in girls and nine to fourteen years in boys), are caused by genetic, environmental, metabolic, ethnic, geographic, nutritional, and economic factors operating through complex regulatory pathways.[3]

1.1 Classification and Etiology of Precocious Puberty

Precocious puberty (PP) is the abnormal early onset of puberty, demonstrated by onset of secondary sexual characteristics before age 8 in girls and age 9 in boys, and results from either independent sex hormone secretion (peripheral/gonadotropin-independent) or premature activation of the hypothalamic-pituitary-gonadal axis (central/gonadotropin-dependent).[4] Central

precocious puberty (CPP), or true/gonadotropin-dependent PP, results from premature activation of this axis; its overall incidence is higher in females, in whom the idiopathic form predominates (80–90% of cases), whereas boys more frequently show organic etiologies (60–70%), including CNS tumors, hydrocephalus, hypothalamic hamartoma, neurofibromatosis type 1, and gain-of-function mutations of the kisspeptin/kisspeptin receptor pathway.[5,6] Peripheral precocious puberty (PPP), or pseudo/gonadotropin-independent PP, is far less prevalent than CPP and results from sex steroid production from gonadal or extragonadal sources independent of gonadotropin stimulation, including McCune-Albright syndrome, familial male-limited PP, congenital adrenal hyperplasia, and rare steroid- or β-hCG-secreting tumors. Incomplete precocious puberty encompasses benign, self-limited variants—premature thelarche, premature adrenarche, and premature menarche—that occasionally progress to complete PP and therefore warrant clinical follow-up.[6]

1.2 Evaluation of Precocious Puberty

Evaluation begins with a thorough personal and family history, including age at onset and progression of pubertal signs, exposure to exogenous sex steroids, and symptoms suggestive of CNS dysfunction.[7] Physical examination should include Tanner staging, assessment for café-au-lait spots suggestive of McCune-Albright syndrome, abdominal examination for masses, ophthalmic and neurological assessment, and evaluation for signs of virilization.[1]

Baseline gonadotropin and sex steroid measurement, supplemented where necessary by a GnRH stimulation test, differentiates CPP (LH rise exceeding FSH) from PPP (prepubertal LH and FSH). Bone age assessment by left hand-wrist radiograph, interpreted against standardized atlases and compared with growth velocity and hormone levels, helps distinguish true PP from benign variants; advancement of more than two years is highly indicative of pathological PP.[8] Brain MRI is the preferred imaging modality for suspected CPP given its superior soft-tissue resolution compared with CT, while pelvic ultrasound and adrenal sonography support evaluation of peripheral causes, including congenital adrenal hyperplasia.[9]

1.3 Management of Precocious Puberty

Gonadotropin-releasing hormone analogs (GnRHa) remain the mainstay of CPP management, suppressing pulsatile endogenous GnRH secretion, stabilizing or reversing pubertal changes, reducing growth velocity to prepubertal levels, and halting bone age progression.[6] Response is monitored clinically and, where needed, hormonally every four to six months, with a hormone test typically performed four months after treatment initiation to confirm efficacy and annual bone age radiography to confirm deceleration of skeletal maturation to less than six months of bone advancement per year;[8] growth hormone co-therapy is considered in selected children who begin treatment before age 10 and continue for more than one year.[10] Management of peripheral precocious puberty targets the underlying source: functional ovarian cysts are usually managed conservatively with clinical and ultrasonographic monitoring; congenital adrenal hyperplasia requires glucocorticoid replacement.[11] and McCune-Albright syndrome is managed with aromatase inhibitors or anti-estrogens such as letrozole or tamoxifen.[12] Isolated premature thelarche and premature adrenarche are generally benign and require only periodic follow-up.[6]

1.4 Rationale of the Study

Despite extensive global literature on precocious puberty, data from Iraq and the wider Middle East remain scarce. Mosul City has faced additional challenges related to nutrition and healthcare access following years of regional conflict, which may influence the epidemiology, presentation, and management of precocious puberty in the local pediatric population, underscoring the need for locally generated evidence.

1.5 Aim of the Study

This study aimed to determine the characteristic features and associated factors of children presenting with precocious puberty at endocrine centers in Mosul City.

1.6 Specific Objectives

- To describe the demographic and clinical characteristics of patients with precocious puberty attending endocrine units in Mosul City.
- To demonstrate the etiological pattern in the study population.
- To identify the first puberty sign among the study sample.
- To clarify treatment adherence among the study population.
- To measure height, weight, BMI, and BMI Z-score among the study population.

2. Subjects and Methods

This cross-sectional study was conducted at the endocrine units of Al-Khansa'a Teaching Hospital and Al-Wafa'a Specialized Medical Center in Mosul City. The study was approved by the local Scientific Council of the Arab Board of Health Specializations in Family Medicine, Iraq, and by the Mosul Ethical Research Committee, Directorate of Health, Nineveh, and approval of the Arab Board of Medical Specialization committee was obtained before the start of the study. Administrations of both centers were informed of the nature and type of the study. The concept and aims of the study were clarified to all participants, and verbal consent was obtained from parents or caregivers; collected data were kept confidential and used only for this study.

A convenience sampling method was used, in which all

patients fulfilling the inclusion criteria during the study period at the two endocrine units were enrolled by the researcher.

2.1 Study Period

Data collection was conducted over six months, from 2 January 2025 to 30 June 2025.

2.2 Sample Size and Study Design

To accomplish the aim of the study, a cross-sectional design was implemented among 94 children diagnosed with precocious puberty by the pediatric specialists at the two endocrine units.

Inclusion criteria: children diagnosed with precocious puberty at the endocrine centers in Mosul City, of all etiological types regardless of treatment status, including both newly and previously diagnosed cases, provided complete medical records and relevant clinical data are available.

Exclusion criteria: children with incomplete or missing medical records that prevented accurate data analysis.

2.3 Data Collection Tool

Data were collected using a detailed questionnaire checklist prepared and administered by the researcher through direct interviews, following verbal consent from parents or caregivers. The questionnaire captured sociodemographic patterns (age, sex, urban/rural residence), potential causative and predisposing factors (family history of early puberty, exposure to endocrine-disrupting substances, underlying medical conditions), and clinical data enabling differentiation between central and peripheral precocious puberty by correlating reported symptoms and history with hormonal and radiological findings.

3. Statistical Analysis

Data collected during the study were summarized in a Microsoft Excel 2007 spreadsheet. IBM-SPSS version 26 was used to perform the statistical analysis, including calculation of means, numbers, percentages, standard deviations, body mass index (BMI), and BMI Z-scores. Data were summarized using proportions and frequencies.

4. RESULTS

The study included 94 patients, comprising 78 females (83%) and 16 males (17%). Table 1 shows the distribution of the study sample according to age group and sex; the majority of cases (47.9%) were aged 7–8 years, comprising 38 females (40.4%) and 7 males (7.4%). Younger age groups (1–6 years) were predominantly female, with no males recorded in the 1–2 and 3–4 year groups, while the 5–6 year group included 24 females and only one male. The 9–10-year group was composed exclusively of males (n=8), with no females recorded in this group.

Table 2 presents the mean height, weight, body mass index (BMI), and BMI Z-scores of girls in the study sample compared with WHO Growth Reference 2007 standards, stratified by age. Mean heights in girls aged 2–3 years were notably below standards, then moderately exceeded standards between ages 4 and 7 years before aligning closely with normative values by age 8 (127.18 cm versus 127 cm). Weight and BMI Z-scores followed a similar two-phase pattern, with markedly elevated values in early childhood (Z=+5.6 at age 3) that progressively declined toward population averages by ages 7–8 (Z=+0.7 and +1.1, respectively). Table 3 presents the corresponding anthropometric comparison for boys, who showed heights and weights above reference standards at ages 6–8 (e.g., height 140.4 cm versus 127 cm at age 8) but below standards by ages 9–10.

Table 1: Distribution of the study sample according to age group and sex.

Age Group	Female n (%)	Male n (%)	Total n (%)
1–2 years	3 (3.2%)	0 (0.0%)	3 (3.2%)
3–4 years	13 (13.8%)	0 (0.0%)	13 (13.8%)
5–6 years	24 (25.5%)	1 (1.1%)	25 (26.6%)
7–8 years	38 (40.4%)	7 (7.4%)	45 (47.9%)
9–10 years	0 (0.0%)	8 (8.5%)	8 (8.5%)
Total	**78 (83.0%)**	**16 (17.0%)**	**94 (100.0%)**

Table 2: Mean height, weight, BMI, and BMI Z-scores in girls of the study sample compared to WHO reference standards, by age.

Age (yrs)	No.	Height (cm)	Standard Height (cm)	Weight (kg)	Standard Weight	BMI	Z-score
2	3	78±1.15	86.00	11.83±1.59	12	19.4	1.7
3	7	79.8±4.47	95.00	18.75±0.48	14	29.4	5.6
4	6	103.8±7.96	102.00	22.0±6.85	16	20.4	3
5	10	110.1±4.99	109.00	22.25±2.20	18	18.4	1.8
6	14	122±2.60	115.00	27.91±2.47	20	18.7	1.8
7	24	125.74±1.82	122.00	26.33±1.31	22	16.6	0.7
8	14	127.18±1.18	127.00	29.11±2.16	25	18	1.1

Table 3: Mean height, weight, BMI, and BMI Z-scores in boys of the study sample compared to WHO reference standards, by age.

Age (yrs)	No.	Height (cm)	Standard Height (cm)	Weight (kg)	Standard Weight	BMI	Z-score
6	1	141±0	115	37±0	20	18.6	1.7
7	1	138±0	122	36±0	23	18.9	1.6
8	6	140.4±4.88	127	44.40±7.50	25	22.5	2.1
9	6	130.2±1.56	133	31.20±3.62	28	18.4	1
10	2	134±1.0	138	41.5±0.5	32	23.1	1.8
Total	**16**	–	–	–	–	–	–

Table 4 shows the distribution of the study sample according to residence, demonstrating that a significant proportion of cases (58.51%) arose from urban areas, with 55 of the 94 cases originating from these regions.

Table 4: Distribution of the study sample according to residence.

Residential Area	No.	Percentage
Urban	55	58.51%
Rural	39	41.49%
Total	94	100.00%

Table 5 presents the distribution of the study sample according to family history of precocious puberty. A positive family history was reported in only 9 patients (9.57%), and all affected cases were female. None of the 16 male patients had a positive family history (0%). Overall, these findings indicate that a family history of precocious puberty was relatively uncommon in the study population and was observed exclusively among female participants.

Table 5: Distribution of the study sample according to family history.

Family History	Female % (No.)	Male % (No.)	Total
Yes	11.54% (9)	0.00% (0)	9 (9.57%)
No	88.46% (69)	100.0% (16)	85 (90.43%)

Table 6 details the etiological distribution of precocious puberty by type, subtype, and sex. Central precocious puberty (CPP) accounted for 74.47% of overall cases, mostly idiopathic (71.28%), while organic/secondary CPP attributed to underlying causes such as tumors or obesity was rare (3.19%) and observed only in girls. Peripheral precocious puberty (PPP) comprised 25.53% of cases, with congenital adrenal hyperplasia (CAH) the most common subtype (21.28%; 13 females and 7 males), whereas isolated premature adrenarche, characterized by pubic hair development without gonadal involvement, was less frequent (4.25%) and observed only in males.

Table 6: Distribution of etiologies of precocious puberty by type, subtype, and sex.

Category	Subcategory	Males	Females	Total	% of Total
Central PP (CPP)	Idiopathic	5	62	67	71.28%
Central PP (CPP)	Organic/Secondary	0	3	3	3.19%
CPP Subtotal	–	5	65	70	74.47%
Peripheral PP (PPP)	CAH-related	7	13	20	21.28%
Peripheral PP (PPP)	Isolated premature adrenarche	4	0	4	4.25%
PPP Subtotal	–	11	13	24	25.53%
Grand Total	–	16	78	94	100%

Table 7 summarizes the first observed puberty signs among the study population, by sex. In females, breast bud development was the most common initial sign (88.46%), with a small proportion (2.56%) presenting with combined breast bud and pubic hair development, suggesting simultaneous onset of multiple signs, while pubic hair alone was the first sign in 8.97% of females. In males, scrotal enlargement was the predominant first sign (62.5%), while pubic hair alone appeared as the first sign in 37.5% of cases.

Table 8 presents the distribution of treatment adherence across age groups and sex. Females showed a high adherence rate overall (87.2%), increasing proportionally with age, while poor adherence among females (12.8%) was concentrated in younger age groups. In contrast, males showed markedly lower adherence (12.5% good adherence versus 87.5% with no follow-up), with poor adherence mainly affecting older children in the 9-and-above age group.

Table 7: Distribution of the first puberty sign among the study population, by sex.

Sex	First Puberty Sign	No.	Percentage
Female	Breast bud	69	88.46%
Female	Breast bud + pubic hair	2	2.56%
Female	Pubic hair only	7	8.97%
Male	Scrotal enlargement	10	62.5%
Male	Pubic hair only	6	37.5%

Table 8: Distribution of treatment adherence across age groups and sex.

Age Range	Female Good Adherence	Female No Follow-Up	Male Good Adherence	Male No Follow-Up	Total
1–2	3	0	0	0	3
3–4	9	4	0	0	13
5–6	24	1	1	0	26
7–8	32	5	1	6	44
9+	0	0	0	8	8
Total	68	10	2	14	94

Overall, these findings characterize the demographic, etiological, anthropometric, and treatment-adherence patterns of precocious puberty among children attending endocrine units in Mosul City.

5. DISCUSSION

The marked female predominance observed in this study (83% versus 17%) is consistent with regional patterns reported by Rohani et al. in Iran, where 86.4% of precocious puberty cases were female, highlighting the role of idiopathic central precocious puberty (CPP) as the primary etiological factor.[13] By contrast, Sørensen et al., studying a Danish population, reported a narrower female-to-male ratio of approximately 3:1.[14], suggesting that regional or ethnic variation—potentially reflecting genetic susceptibility, environmental influences, and differences in healthcare-seeking behavior—may affect the presentation of CPP.

The predominance of cases in the 7–8 year age group, comprising nearly half of the sample, parallels findings by Stagi et al., who documented a similar predominance (approximately 48%) among 224 Italian girls referred for suspected precocious puberty during and after the COVID-19 lockdown, with a mean age at diagnosis of 7.5 ± 1.2 years.[15] The complete absence of males in the youngest age groups (1–4 years) and their exclusive presence in the 9–10 year group reflect gender-specific patterns in onset and presentation, consistent with Bangalore and Rani, who reported that boys typically present later and with more severe forms of precocious puberty.[16] However, a Danish registry study by Bräuner et al. covering 1998–2019 found that precocious puberty is increasing in both sexes, with more boys now developing idiopathic (non-pathological) disease, likely reflecting environmental factors such as obesity and chemical exposures,[17] suggesting that modern lifestyle and environmental influences may be reshaping the traditional view that early puberty in boys chiefly signals pathological causes.

The anthropometric patterns observed among girls in this study—initial growth delay in the youngest children followed by height and weight acceleration and a return toward normative values by age 8—mirror the recognized pathophysiology of estrogen-driven epiphyseal maturation. Latronico et al. similarly reported that early activation of the HPG axis initially accelerates growth but ultimately causes premature skeletal maturation and reduced adult height.[18] The very high BMI Z-scores observed in the youngest girls (Z=+5.6 at age 3) suggest an early propensity toward overweight potentially related to hyperandrogenism or insulin resistance, with the later transient normalization by ages 7–8 possibly reflecting redistribution of body mass during peak growth velocity, changes that may carry implications for future cardiovascular and metabolic risk.[19]

Boys with precocious puberty in this study displayed an early growth spurt with markedly taller stature at ages 6–8, followed by a deceleration and subnormal height by ages 9–10, consistent with the biphasic growth pattern described by Aguirre and Eugster, who noted that bone age often exceeds chronological age by one to two years in affected boys, producing initial tall stature that may nonetheless compromise final adult height if untreated.[20] The elevated weights observed across most ages in boys likely reflect increased adiposity and muscle mass driven by early sex-steroid exposure; Jang et al. similarly reported strong associations between endogenous sex hormones and adiposity across youth weight categories, consistent with an increased obesity risk associated with precocious puberty more broadly[21] The very small male sample size in this study, particularly the single participants recorded at ages 6 and 7, limits the generalizability of these findings and warrants cautious interpretation.

The predominance of urban cases (58.5%) observed in this study aligns with research by López-Rodríguez et al., who noted that endocrine-disrupting chemicals are often more prevalent in urban environments and may accelerate pubertal onset.[22] Liu et al., in a school-based

study among Chinese children, similarly found that lifestyle factors and modern dietary habits—including increased consumption of processed foods and high-calorie diets—play a significant role in the early onset of puberty, a pattern plausibly relevant to urban populations in Mosul.[23]

The low prevalence of a positive family history in this study (9.6%, all females) suggests a limited genetic contribution in this population, or possibly under-recognition of familial patterns. Canton et al. identified imprinted genes such as MKRN3, DLK1, and MECP2 as more commonly implicated in girls with familial or idiopathic CPP, noting that most cases nonetheless remain sporadic, suggesting that environmental triggers may augment genetic susceptibility rather than acting through direct heredity.[24] The predominance of negative family histories in this sample (90.4%) similarly points toward modifiable risk factors, such as obesity and endocrine disruptors, as more relevant contributors than heredity in this population.

Central precocious puberty predominated in this study (74.5%), mainly idiopathic (71.3%), consistent with global patterns in which CPP constitutes 70–90% of early puberty cases; Latronico et al. reported that CPP accounts for approximately 80–90% of cases in girls and 50–60% in boys, with idiopathic forms most common, especially among girls.[18] Organic CPP was rare in this sample (3.2%) and observed exclusively in girls, which contrasts with Vurallı et al., who reported organic CPP to be 3.5 times more common in boys than girls in a Turkish cohort and recommended careful evaluation of boys with early puberty for underlying organic causes;[5] the absence of organic CPP among boys in the present study may reflect the small male sample size or under-diagnosis. Peripheral precocious puberty accounted for 25.5% of cases, with congenital adrenal hyperplasia as the leading subtype (21.3%), comparable to findings from Saudi Arabia by Al-Jurayyan et al., where CAH was similarly the leading cause of peripheral precocious puberty.[25]

Breast budding was the initial sign in 88.5% of girls and scrotal enlargement in 62.5% of boys, closely mirroring the review by Cheuiche et al., who reported thelarche as the presenting sign in up to 90% of girls with CPP and testicular enlargement in 60–70% of boys.[26] A small proportion of girls (2.6%) presented with simultaneous thelarche and pubic hair development, a pattern highlighted by Augsburger et al. as warranting further investigation into mixed central and peripheral contributions.[27] Isolated pubic hair as the presenting sign was noted in 9.0% of girls, comparable to the 12.5% reported by Sarıkaya and Kilci among Turkish girls,[28] but was considerably more common among boys in this study (37.5%) than the 2–10% reported by Augsburger et al., possibly reflecting increased adrenal involvement such as congenital adrenal hyperplasia or region-specific genetic and environmental factors.[27]

Treatment adherence differed markedly by sex, with girls showing high adherence (87.2%) that improved with age, while boys showed predominantly poor adherence (87.5% with no follow-up), particularly among those aged nine years and older. Comparable adherence rates among girls were reported by Yang et al. in a Chinese cohort with central precocious puberty (76%), who identified caregiver education, understanding of treatment importance, and financial constraints as key influencing factors that may similarly underlie the age-related adherence patterns observed here.[29] Adherence among boys with precocious puberty remains poorly studied in the literature, and the pronounced non-adherence observed in this study may reflect stigma, lower perceived need for treatment, or diagnostic delay, warranting further targeted investigation given the small male sample size in this study.

This study is limited by its cross-sectional, single-region design and the small number of male participants, which restricts the generalizability of sex-based comparisons and precludes causal inference regarding etiological or environmental associations.

Taken together, these findings carry practical implications for endocrine services in resource-limited, post-conflict settings such as Mosul City: early recognition of breast budding or scrotal enlargement, prompt hormonal and radiological evaluation, and structured follow-up protocols tailored separately to girls and boys may help narrow the observed gender gap in diagnosis and treatment adherence, while population-level attention to urban environmental exposures and childhood nutrition may help address modifiable contributors to idiopathic disease.

6. CONCLUSION AND RECOMMENDATIONS

This study demonstrates a clear female predominance among children with precocious puberty in Mosul City, with idiopathic central precocious puberty as the leading etiology, while boys presented at older ages and were more often affected by peripheral causes such as congenital adrenal hyperplasia. Peak incidence occurred at 7–8 years, consistent with global data, and most cases arose from urban areas with a low prevalence of family history, supporting a predominant role for environmental and modifiable risk factors over heredity. Anthropometric findings revealed early overweight and elevated BMI Z-scores in younger girls, with eventual epiphyseal closure limiting final height, while boys showed early height and weight acceleration followed by deceleration attributed to advanced bone age; both patterns indicate increased risk of obesity and associated metabolic and cardiovascular sequelae. Treatment adherence was markedly better among girls than boys, likely reflecting cultural factors or delays in diagnosing boys, while conflict-related nutritional and healthcare access challenges in Mosul City may further compound these risks.

Regular monitoring of children's growth using WHO standards is recommended, particularly for children with rapid growth spurts. Poor treatment adherence among boys should be addressed through culturally sensitive education programs for families and healthcare providers. Public health campaigns promoting healthy diets and physical activity and reducing exposure to endocrine-disrupting chemicals should be developed, particularly in urban areas, and local exposure to such chemicals and obesity-related factors in Mosul should be further studied given their potential role in idiopathic central precocious puberty. Future analytic studies, such as cohort or case-control designs, are recommended to identify specific causative risk factors for precocious puberty in Mosul City.

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